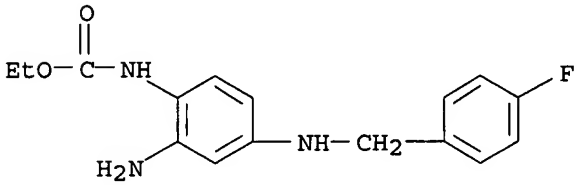
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 150812-12-7 REGISTRY
CN Carbamic acid, [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN D 23129
CN Ethyl [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]carbamate
CN **Retigabine**
FS 3D CONCORD
MF C16 H18 F N3 O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMLIST, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

49 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
51 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 1 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:566612 CAPLUS
TITLE: Effect of the KCNQ potassium channel opener retigabine on single KCNQ2/3 channels expressed in CHO cells
AUTHOR(S): Tatulian, L.; Brown, D. A.
CORPORATE SOURCE: Department of Pharmacology, University College London, London, WC1E 6BT, UK
SOURCE: Journal of Physiology (Cambridge, United Kingdom) (2003), 549(1), 57-63
CODEN: JPHYA7; ISSN: 0022-3751
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB KCNQ2/3 potassium channel subunits were co-expressed in Chinese hamster ovary (CHO) cells and currents through single channels recorded using cell-attached patches. Channels had a similar slope conductance in the presence (8.04 .+-. 0.02 pS) and absence (7.6 .+-. 0.01 pS) of 10 .mu.M retigabine. The mean maximal open probability (Po) for single KCNQ2/3 channels was 0.13 .+-. 0.02, with a half-maximal Po potential (Vo) of -28.7 .+-. 1.4 mV for control recordings. Retigabine increased mean maximal Po to 0.38 .+-. 0.04 and produced a hyperpolarizing shift of Vo to -40.1 .+-. 3.4 mV. Single KCNQ2/3 channels have multiple voltage-dependent kinetic components in their activity (CL-OS-CM-OL-CS; C = closed, O = open, L = long, S = short, M = medium), giving short, medium and long closed times (.tau.CS, .tau.CM, .tau.CL) and short and long open times (.tau.OS and .tau.OL). In the presence of retigabine at 0 mV, the combined duration and contributions of the longest closed time .tau.CL decreased tenfold, while the short and long open times increased fourfold and twofold, resp. Thus, steady-state kinetics were modified to favor the open channel configuration.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN TH

L5 ANSWER 3 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:164709 CAPLUS
DOCUMENT NUMBER: 139:78965
TITLE: Synergy between Retigabine and GABA in modulating the convulsant site of the GABAA receptor complex
AUTHOR(S): van Rijn, Clementina M.; Willems-van Bree, Elly
CORPORATE SOURCE: NICI/Department of Biological Psychology, University of Nijmegen, Nijmegen, 6500 HE, Neth.
SOURCE: European Journal of Pharmacology (2003), 464(2-3), 95-100
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mol. mechanism underlying the activity of the novel antiepileptic drug Retigabine is not yet fully understood. The aim of this study was to investigate whether Retigabine interacts directly with the GABAA receptor complex (.gamma.-aminobutyric acid). Receptor-binding assays were conducted using rat brain membranes. [3H]-t-Butyl-bicyclo-orthobenzoate ([3H]TBOB) was used as a tracer ligand. The authors detd. the effects of GABA and Retigabine in the presence of several concns. of GABA on the binding of [3H]TBOB. GABA inhibited [3H]TBOB binding with an EC50 of 4.8 .mu.M. In the absence of GABA, Retigabine inhibited [3H]TBOB with an EC50 of 124 .mu.M and an EC50 of 42 .mu.M in the presence of 2.5 .mu.M GABA. Isobolic anal. revealed that Retigabine acts in synergy with GABA in displacing [3H]TBOB. This synergy could be quantified by a mol. model in which GABA and Retigabine both allosterically displace [3H]TBOB, and Retigabine allosterically enhances the binding of GABA and vice versa with a factor of 4. In summary, the authors found that Retigabine does indeed interact with a site on the GABAA receptor complex, and this site is pos. allosterically coupled with the GABA site. This GABA-pos. effect may well contribute to the clin. anticonvulsive effects of Retigabine.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABL

5 ANSWER 10 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:793402 CAPLUS
DOCUMENT NUMBER: 137:289015
TITLE: Methods using KCNQ potassium channel agonists for treating hyperactive gastric motility
INVENTOR(S): Argentieri, Thomas Michael
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080898	A2	20021017	WO 2002-US10268	20020402
WO 2002080898	A3	20030821		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002183395	A1	20021205	US 2002-114148	20020402

PRIORITY APPLN. INFO.: US 2001-281471P P 20010404
OTHER SOURCE(S): MARPAT 137:289015
AB The invention provides methods and pharmaceutical compns. for treating, inhibiting, or preventing hyperactive gastric motility in a mammal, using agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be assocd. with maladies including colitis, irritable bowel syndrome, and Crohn's disease. Compds. useful in these methods include the 1,2,4-triaminobenzene derivs. described in U.S. Patent No. 5,384,330 (Dieter et al.) and the substituted 3-Ph oxindole compds. described in U.S. Patent No. 5,565,483 (Hewawasam et al.). Among the preferred compds. of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid Et ester, also referred to as retigabine.

L5 ANSWER 11 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN

L5 ANSWER 10 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:793402 CAPLUS
DOCUMENT NUMBER: 137:289015
TITLE: Methods using KCNQ potassium channel agonists for treating hyperactive gastric motility
INVENTOR(S): Argentieri, Thomas Michael
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080898	A2	20021017	WO 2002-US10268	20020402
WO 2002080898	A3	20030821		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002183395	A1	20021205	US 2002-114148	20020402

PRIORITY APPLN. INFO.: US 2001-281471P P 20010404
OTHER SOURCE(S): MARPAT 137:289015
AB The invention provides methods and pharmaceutical compns. for treating, inhibiting, or preventing hyperactive gastric motility in a mammal, using agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be assocd. with maladies including colitis, irritable bowel syndrome, and Crohn's disease. Compds. useful in these methods include the 1,2,4-triaminobenzene derivs. described in U.S. Patent No. 5,384,330 (Dieter et al.) and the substituted 3-Ph oxindole compds. described in U.S. Patent No. 5,565,483 (Hewawasam et al.). Among the preferred compds. of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid Et ester, also referred to as retigabine.

L5 ANSWER 11 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:696658 CAPLUS
DOCUMENT NUMBER: 137:210975
TITLE: Modulators of KCNQ potassium channels and use thereof in treating migraine and mechanistically related diseases
INVENTOR(S): Dworetzky, Steven I.; Gribkoff, Valentin K.; Kinney, Gene G.; Hewawasam, Piyasena
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002128277	A1	20020912	US 2002-75703	20020214
WO 2002072088	A2	20020919	WO 2002-US4374	20020214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-269967P P 20010220

AB Compds. which function as modulators, particularly, openers, of human KCNQ potassium channel proteins or polypeptides, particularly, central nervous system (CNS)-located KCNQ potassium channels, and heteromultimers thereof, and their use in the treatment of migraine are provided by the present invention. One novel type of potassium channel polypeptide openers provided by the present invention is the fluorooxindole compds., described for the first time as therapeutics for the treatment of migraine by preventing the asynchronous firing of neurons. Other KCNQ potassium channel opener compds. that are also useful in the treatments of the invention include 2,4-disubstituted pyrimidine-5-carboxamide derivs. One or more of the compds. according to the present invention may be utilized alone, in combination, or in conjunction with other treatment modalities for reducing, ameliorating and/or alleviating migraine or diseases similar to, or mechanistically related to, migraine, e.g., cluster headache.

L5 ANSWER 12 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:487384 CAPLUS
DOCUMENT NUMBER: 137:68158
TITLE: Phenylcarbamates for treating anxiety disorders
INVENTOR(S): Bowlby, Mark Robert; Rosenzweig-Lipson, Sharon Joy
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002049628	A2	20020627	WO 2001-US49362	20011219
WO 2002049628	A3	20021017		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002111379	A1	20020815	US 2001-22579	20011217
US 6589986	B2	20030708		
AU 2002031122	A5	20020701	AU 2002-31122	20011219
EP 1343495	A2	20030917	EP 2001-991398	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-256834P P 20001220
WO 2001-US49362 W 20011219

OTHER SOURCE(S): MARPAT 137:68158
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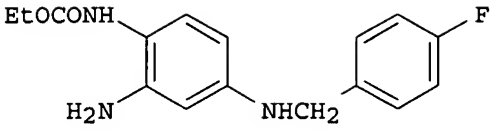

I

AB This invention provides methods for treating, preventing or inhibiting anxiety, anxiety-related conditions and phobias in a mammal using phenylcarbamates such as retigabine (I). Capsules were prepd. contg. I.

L5 ANSWER 13 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:267400 CAPLUS
DOCUMENT NUMBER: 137:134965
TITLE: Effects of the anticonvulsant retigabine on cultured cortical neurons: changes in electroresponsive properties and synaptic transmission
AUTHOR(S): Otto, James F.; Kimball, Matthew M.; Wilcox, Karen S.
CORPORATE SOURCE: Anticonvulsant Drug Development Program, Department of Pharmacology and Toxicology, University of Utah, Salt Lake City, UT, USA
SOURCE: Molecular Pharmacology (2002), 61(4), 921-927
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The whole-cell patch-clamp technique was used to examine the effects of retigabine, a novel anticonvulsant drug, on the electroresponsive properties of individual neurons as well as on neurotransmission between monosynaptically connected pairs of cultured mouse cortical neurons. Consistent with its known action on potassium channels, retigabine significantly hyperpolarized the resting membrane potentials of the neurons, decreased input resistance, and decreased the no. of action potentials generated by d.c. injection. In addn., retigabine potentiated inhibitory postsynaptic currents (IPSCs) mediated by activation of .gamma.-aminobutyric acidA (GABAA) receptors. IPSC peak amplitude, 90-to-10% decay time, weighted decay time const., slow decay time const., and, consequently, the total charge transfer were all significantly enhanced by retigabine in a dose-dependent manner. This effect was limited to IPSCs; retigabine had no significant effect on excitatory postsynaptic currents (EPSCs) mediated by activation of non-N-methyl-D-aspartate ionotropic glutamate receptors. A form of short-term presynaptic plasticity, paired-pulse depression, was not altered by retigabine, suggesting that its effect on IPSCs is primarily postsynaptic. Consistent with the hypothesis that retigabine increases inhibitory neurotransmission via a direct action on the GABAA receptor, the peak amplitudes, 90-to-10% decay times, and total charge transfer of spontaneous miniature IPSCs were also significantly increased. Therefore, retigabine potently reduces excitability in neural circuits via a synergistic combination of mechanisms.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:141657 CAPLUS
DOCUMENT NUMBER: 137:194934
TITLE: Multiple-dose, linear, dose-proportional pharmacokinetics of retigabine in healthy volunteers
AUTHOR(S): Ferron, Geraldine M.; Paul, Jeffrey; Fruncillo, Richard; Richards, Lyette; Knebel, Norbert; Getsy, John; Troy, Steven
CORPORATE SOURCE: Wyeth-Ayerst Research, Philadelphia, PA, 19101, USA

SOURCE: Journal of Clinical Pharmacology (2002), 42(2), 175-182
CODEN: JCPCBR; ISSN: 0091-2700
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retigabine, a first-in-class selective M-current potassium channel opener, is a novel antiepileptic compd. currently in clin. development. The purpose of this randomized placebo-controlled study was to assess retigabine oral safety and pharmacokinetics in healthy male volunteers (N = 45). Subjects received one dose on day 1 and doses every 12 h for the next 14 days. Fixed doses were given to the first four groups (200, 400, 500, and 600 mg per day). Titrated doses were given to group 5 in 100 mg increases every 4 days, achieving 700 mg per day on day 15. Serial blood samples were collected on days 1 and 15. Pharmacokinetic parameters were compared between days and among dose groups. After administration f a single dose, retigabine was rapidly absorbed, with max. concns. of 387 ng/mL (normalized to a 100 mg dose) occurring within 1.5 h. Retigabine was eliminated with a mean terminal half-life of 8.0 h and an apparent oral clearance of 0.70 L/h/kg in white subjects. In black subjects, retigabine clearance and vol. of distribution were 25% and 30% lower, resp., after normalizing by body wt., leading to higher exposure in this population. Retigabine's pharmacokinetics was linearly dose proportional. Steady-state pharmacokinetics was in agreement with single-dose pharmacokinetics, and the accumulation ratio was about 1.5. Retigabine and AWD21-360 trough evening concns. were significantly lower (about 30% to 35%) than morning values. The titrn. regimen allowed for higher doses to be tolerated compared to the fixed-dose regimen. In conclusion, the pharmacokinetics of retigabine is linearly dose proportional for daily doses of 100 to 700 mg and is not modified on multiple administrations.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:134217 CAPLUS
DOCUMENT NUMBER: 136:178017
TITLE: Use of KCNQ potassium channel agonists for treating bladder incontinence
INVENTOR(S): Argentieri, Thomas Michael; Sheldon, Jeffrey Howard; Bowlby, Mark R.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6348486	B1	20020219	US 2001-977828	20011015
WO 2002032419	A2	20020425	WO 2001-US32204	20011016
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002011758	A5	20020429	AU 2002-11758	20011016
EP 1326597	A2	20030716	EP 2001-979836	20011016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002032960	A2	20020425	WO 2001-US32371	20011017
WO 2002032960	A3	20030417		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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AU 2002013308	A5	20020429	AU 2002-13308	20011017
EP 1328550	A2	20030723	EP 2001-981678	20011017
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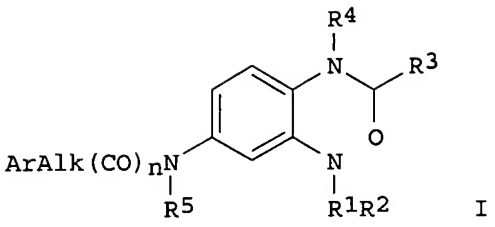
NO 2003001580	A	20030614	NO 2003-1580	20030408

PRIORITY APPLN. INFO.:
US 2000-241078P P 20001017
US 2001-281428P P 20010404
WO 2001-US32204 W 20011016
WO 2001-US32371 W 20011017

OTHER SOURCE(S): MARPAT 136:178017
GI



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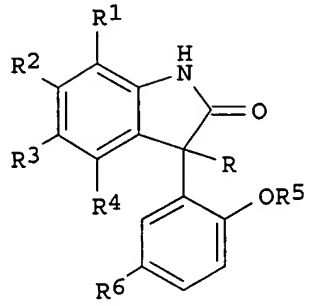

II

AB The invention provides methods and pharmaceutical compns. for maintaining bladder control or treating urinary incontinence in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The invention include compds. of formula, I [R1= H, alkyl(C1-C6), alkanoyl(C2-C6), or Aryl radical; R2= H, alkyl(C1-C6); R3= alkoxy, alkylamino, dialkylamino (C1-C6), amino or amino substituted by alkyl (C1-C6), alkenyl, alkynyl (C2-C6), the Aryl or Aryloxy radical; R4, R5 = H, alkyl(C1-C6) or Aryl radical]. The invention also discloses compds. of the type, II [R= H, OH, F; R1, R2, R3,R4 = H, alkyl(C1-C4), halogen, CF3, Ph, p-CH3Ph, p-CF3Ph; R1, R2, R3,R4 form a fused benzo ring; R5= H, alkyl(C1-C4); R6= Cl, CF3]. Compds. useful in these methods include the 1,2,4-triamino-benzene derivs. described in U.S. Pat. No. 5,384,330 (Dieter et al.) and the substituted 3-Ph oxindole compds. described in U.S. Pat. No. 5,565,483 (Hewawasam et al.). Among the preferred compds. of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid Et ester, also referred to as retigabine.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:676572 CAPLUS
DOCUMENT NUMBER: 135:216020
TITLE: Controlled release oral drug delivery systems containing sucrose fatty acid esters
INVENTOR(S): Hoffmann, Torsten; Pieroth, Michael; Zessin, Gerhard; Landgraf, Karl-Friedrich
PATENT ASSIGNEE(S): Awd. Pharma G.m.b.H. and Co. K.-G., Germany
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066081	A2	20010913	WO 2001-EP2500	20010306

WO 2001066081 A3 20020314
W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR
DE 10010509 A1 20010913 DE 2000-10010509 20000308
US 2002015730 A1 20020207 US 2001-793936 20010227
EP 1267828 A2 20030102 EP 2001-923641 20010306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR
BR 2001009036 A 20030318 BR 2001-9036 20010306
JP 2003528829 T2 20030930 JP 2001-564734 20010306
NO 2002004237 A 20020905 NO 2002-4237 20020905
BG 107064 A 20030430 BG 2002-107064 20020905
PRIORITY APPLN. INFO.: DE 2000-10010509 A 20000308
US 2000-187962P P 20000309
WO 2001-EP2500 W 20010306

AB The invention relates to novel oral pharmaceutical formulations having a variably adjustable release effect. The formulations contain one or several sucrose fatty acid esters as exclusive release control agents, in addn. to one or several active ingredients. Saccharose fatty acid esters are mixed with the active ingredient and are also used addnl. to coat the formulation. The invention also relates to a method for the prodn. of the formulations by fusion granulation or fusion pelletizing. The pharmaceutical formulations range from quick release to delayed release drugs. Thus 400 g tramadol hydrochloride and 400 g saccharose ester stearate (HLB value = 1) were mixed with 700 rpm and disintegrated with 3000 rpm at 55.degree.C; the produced granules were sieved through a 1.4 mm mesh.

L5 ANSWER 17 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:676154 CAPLUS
DOCUMENT NUMBER: 135:216014
TITLE: Controlled release oral drug delivery systems containing sucrose fatty acid esters
INVENTOR(S): Hoffmann, Torsten; Pieroth, Michael; Zessin, Gerhard; Landgraf, Karl-Friedrich
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden G.m.b.H., Germany
SOURCE: Ger. Offen., 48 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10010509	A1	20010913	DE 2000-10010509	20000308
WO 2001066081	A2	20010913	WO 2001-EP2500	20010306
WO 2001066081	A3	20020314		
W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1267828	A2	20030102	EP 2001-923641	20010306
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
BR 2001009036	A	20030318	BR 2001-9036	20010306
JP 2003528829	T2	20030930	JP 2001-564734	20010306
CA 2339913	AA	20010908	CA 2001-2339913	20010307
ZA 2002007050	A	20021120	ZA 2002-7050	20020903
NO 2002004237	A	20020905	NO 2002-4237	20020905

BG 107064 A 20030430 BG 2002-107064 20020905
PRIORITY APPLN. INFO.: DE 2000-10010509 A 20000308
US 2000-187962P P 20000309
WO 2001-EP2500 W 20010306

AB The invention relates to oral pharmaceutical formulations having a variably adjustable release effect. The formulations contain one or several sucrose fatty acid esters as exclusive release control agents, in addn. to one or several active ingredients. Saccharose fatty acid esters are mixed with the active ingredient and are also used addnl. to coat the formulation. The invention also relates to a method for the prodn. of the formulations by fusion granulation or fusion pelletizing. The pharmaceutical formulations range from quick release to delayed release drugs. Thus 400 g tramadolhydrochloride and 400 g saccharose ester stearate (HLB value = 1) were mixed with 700 rpm and disintegrated with 3000 rpm at 55.degree.C; the produced granules were sieved through a 1.4 mm mesh.

L5 ANSWER 18 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:549341 CAPLUS
DOCUMENT NUMBER: 135:313545
TITLE: Activation of expressed KCNQ potassium currents and native neuronal M-type potassium currents by the anti-convulsant drug retigabine
AUTHOR(S): Tatulian, L.; Delmas, P.; Abogadie, F. C.; Brown, D. A.
CORPORATE SOURCE: Department of Pharmacology, University College London, London, WC1E 6BT, UK
SOURCE: Journal of Neuroscience (2001), 21(15), 5535-5545
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retigabine [D-23129; N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid Et ester] is a novel anticonvulsant compd. that is now in clin. phase II development. It has previously been shown to enhance currents generated by KCNQ2/3 K+ channels when expressed in Chinese hamster ovary (CHO) cells. In the present study, the authors have compared the actions of retigabine on KCNQ2/3 currents with those on currents generated by other members of the KCNQ family (homomeric KCNQ1, KCNQ2, KCNQ3, and KCNQ4 channels) expressed in CHO cells and on the native M current in rat sympathetic neurons (thought to be generated by KCNQ2/3 channels). Retigabine produced a hyperpolarizing shift of the activation curves for KCNQ2/3, KCNQ2, KCNQ3, and KCNQ4 currents with differential potencies in the following order: KCNQ3 > KCNQ2/3 > KCNQ2 > KCNQ4, as measured either by the max. hyperpolarizing shift in the activation curves or by the EC50 values. In contrast, retigabine did not enhance cardiac KCNQ1 currents. Retigabine also produced a hyperpolarizing shift in the activation curve for native M channels in rat sympathetic neurons. The retigabine-induced current was inhibited by muscarinic receptor stimulation, with similar agonist potency but 25% reduced max. effect. In unclamped neurons, retigabine produced a hyperpolarization and reduced the no. of action potentials produced by depolarizing current injections, without change in action potential configuration.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:389379 CAPLUS
DOCUMENT NUMBER: 135:221181
TITLE: KCNQ4 channel activation by BMS-204352 and retigabine
AUTHOR(S): Schroder, R. L.; Jespersen, T.; Christophersen, P.; Strobaek, D.; Jensen, B. S.; Olesen, S.-P.
CORPORATE SOURCE: NeuroSearch A/S, Ballerup, DK 2750, Den.
SOURCE: Neuropharmacology (2001), 40(7), 888-898

CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of potassium channels generally reduces cellular excitability, making potassium channel openers potential drug candidates for the treatment of diseases related to hyperexcitability such as epilepsy, neuropathic pain, and neurodegeneration. Two compds., BMS-204352 and retigabine, presently in clin. trials for the treatment of stroke and epilepsy, resp., have been proposed to exert their protective action via an activation of potassium channels. Here we show that KCNQ4 channels, stably expressed in HEK293 cells, were activated by retigabine and BMS-204352 in a reversible and concn.-dependent manner in the concn. range 0.1-10 .mu.M. Both compds. shifted the KCNQ4 channel activation curves towards more neg. potentials by about 10 mV. Further, the maximal current obtainable at large pos. voltages was also increased concn.-dependently by both compds. Finally, a pronounced slowing of the deactivation kinetics was induced in particular by BMS-204352. The M-current blocker linopirdine inhibited the baseline current, as well as the BMS-204352-induced activation of the KCNQ4 channels. KCNQ2, KCNQ2/Q3, and KCNQ3/Q4 channels were activated to a similar degree as KCNQ4 channels by 10 .mu.M of BMS-204352 and retigabine, resp. The compds. are, thus, likely to be general activators of M-like currents.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 20 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:293195 CAPLUS
DOCUMENT NUMBER: 136:210388
TITLE: Effects of retigabine on rhythmic synchronous activity of human neocortical slices
AUTHOR(S): Straub, H.; Kohling, R.; Hohling, J.-M.; Rundfeldt, C.; Tuxhorn, I.; Ebner, A.; Wolf, P.; Pannek, H.; Speckmann, E.-J.
CORPORATE SOURCE: Institut fur Physiologie, Universitat Munster, Munster, D-48149, Germany
SOURCE: Epilepsy Research (2001), 44(2-3), 155-165
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiepileptic effects of the novel antiepileptic drug retigabine (D-23129) [N-(2-amino-4-(4-flurobenzylamino)phenyl) carbamic acid Et ester] were tested in neocortical slice prepns. (n=23) from 17 patients (age, 3-42 yr) who underwent surgery for the treatment of intractable epilepsy. Epileptiform events consisted of spontaneously occurring rhythmic sharp waves, as well as of epileptiform field potentials (EFP) elicited by superfusion with Mg2+-free soln. without or with addn. of 10 .mu.mol/l bicuculline. (1) Spontaneous rhythmic sharp waves (n=6), with retigabine application, the repetition rate was decreased down to 12-47% of initial value (10 .mu.mol/l, n=3) after 180 min or suppressed completely within 12 min (50 .mu.mol/l, n=3). (2) Low Mg2+ EFP (n=9), with retigabine application, the repetition rate was decreased down to 50 and 65% of initial value (10 .mu.mol/l; n=2) after 180 min or suppressed completely after 9-55 min (10, 50 and 100 .mu.mol/l; n=2 in each case). In one slice only a transient redn. of the repetition rate was seen with 10 .mu.mol/l retigabine. (3) Low Mg2+ EFP with addn. of bicuculline (n=8), with retigabine application, the repetition rate was decreased down to 12-55% of initial value (10 .mu.mol/l; n=4) after 180 min or suppressed completely after 6-30 min (50 and 100 .mu.mol/l; n=2 in each case). The depressive effect of retigabine was reversible in all but one slice. The results show a clear antiepileptic effect of retigabine in human neocortical slices on spontaneously occurring rhythmic sharp waves and different types of induced seizure activity.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:139982 CAPLUS
DOCUMENT NUMBER: 135:28669
TITLE: Influence of retigabine on the anticonvulsant activity of some antiepileptic drugs against audiogenic seizures in DBA/2 mice
AUTHOR(S): De Sarro, Giovambattista; Di Paola, Eugenio Donato; Conte, Giuseppe; Pasculli, Maria Patrizia; De Sarro, Angela
CORPORATE SOURCE: Chair of Pharmacology, Department of Experimental and Clinical Medicine, Faculty of Medicine and Surgery, Policlinico Mater Domini, University of Catanzaro, Catanzaro, 88100, Italy
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2001), 363(3), 330-336
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retigabine (D-2319, 0.5-20 mg/kg i.p.) antagonized dose dependently audiogenic seizures in DBA/2 mice. Retigabine at 0.5 mg/kg i.p., a dose that per se did not affect the occurrence of audiogenic seizures significantly, potentiated the anticonvulsant activity of carbamazepine, diazepam, felbamate, lamotrigine, phenytoin, phenobarbital and valproate against sound-induced seizures in DBA/2 mice. The degree of additivity for the effect induced by retigabine was greatest for diazepam, phenobarbital, phenytoin and valproate, less for carbamazepine and lamotrigine and least for felbamate. The increase in anticonvulsant activity was usually assocd. with a comparable increase in motor impairment. However, the therapeutic index of combined treatment (drugs plus retigabine), was more favorable than the same drug plus vehicle. Since retigabine had no significant influence on the total and free plasma levels of the anticonvulsant drugs, pharmacokinetic interactions, in terms of total or free plasma levels, are not probable. However, the possibility that retigabine modifies the clearance of the anticonvulsant drugs from the brain cannot be excluded. Retigabine had no significant effect on the hypothermic effects of the anticonvulsants tested. In conclusion, retigabine showed an additive effect when administered in combination with classical anticonvulsants, most notably diazepam, phenobarbital, phenytoin and valproate.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:120379 CAPLUS
DOCUMENT NUMBER: 134:305233
TITLE: Characterization of KCNQ5/Q3 potassium channels expressed in mammalian cells
AUTHOR(S): Wickenden, Alan D.; Zou, Anruo; Wagoner, P. Kay; Jegla, Tim
CORPORATE SOURCE: ICAgen Inc., Durham, NC, 27703, USA
SOURCE: British Journal of Pharmacology (2001), 132(2), 381-384
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heteromeric KCNQ5/Q3 channels were stably expressed in Chinese Hamster ovary cells and characterized using the whole cell voltage-clamp technique. KCNQ5/Q3 channels were activated by the novel anticonvulsant, retigabine (EC50 1.4 .mu.M) by a mechanism that involved drug-induced,

leftward shifts in the voltage-dependence of channel activation (-31.8 mV by 30 .mu.M retigabine). KCNQ5/Q3 channels were inhibited by linopirdine (IC50 7.7 .mu.M) and barium (IC50 0.46 mM), at concns. similar to those required to inhibit native M-currents. These findings identify KCNQ5/Q3 channels as a mol. target for retigabine and raise the possibility that activation of KCNQ5/Q3 channels may be responsible for some of the anti-convulsant activity of this agent. Furthermore, the sensitivity of KCNQ5/Q3 channels to linopirdine supports the possibility that potassium channels comprised of KCNQ5 and KCNQ3 may make a contribution to native M-currents.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:101418 CAPLUS
DOCUMENT NUMBER: 134:141715
TITLE: Potassium channel modulatory binding site, and use in drug screening
INVENTOR(S): Rundfeldt, Chris; Netzer, Rainer
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GMBH, Germany
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009612	A1	20010208	WO 2000-EP7348	20000729
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6472165	B1	20021029	US 1999-368314	19990803
EP 1200831	A1	20020502	EP 2000-949423	20000729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY				
JP 2003506050	T2	20030218	JP 2001-514572	20000729

PRIORITY APPLN. INFO.: US 1999-368314 A 19990803
WO 2000-EP7348 W 20000729

AB The invention concerns a selective modulatory binding site on the potassium channel with the subunits KCNQ2 and KCNQ3 that are identified by retigabine. The binding site can be used to screen for substances for treating diseases that are related to a hyperexcitability or a hypoexcitability of neuronal cells.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 24 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:96209 CAPLUS
DOCUMENT NUMBER: 135:146474
TITLE: Retigabine (ASTA medica)
AUTHOR(S): Fatope, Majekodunmi O.
CORPORATE SOURCE: College of Science, Sultan Qaboos University, Ai-Khod, Oman
SOURCE: IDrugs (2001), 4(1), 93-98
CODEN: IDRUFN; ISSN: 1369-7056
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 80 refs. ASTA Medica is developing retigabine, a carbamic acid Et ester and a selective potassium channel opener, for the treatment

of complex partial seizures. Phase II trials have commenced [249117], and a multicenter placebo-controlled dosage-finding study has begun in Europe and Australia [392702]. Retigabine is also undergoing phase II testing in Germany, Switzerland, Russia and the US for the potential treatment of epilepsy [323383]. Phase II trials have shown >50% redn. in seizure frequency in 12 of 35 patients with refractory epilepsy [373379]. Phase I clin. trials for epilepsy were successfully completed in Germany in 1995 [180371]. Single and multiple dose trials demonstrated the tolerability and favorable pharmacokinetic behavior of the compd. [264306]. The compd. showed good compatibility and exhibits an antisense anticonvulsive effect in various preclin. epilepsy models [250565,299344]. Side effects of mild to moderate tiredness, fatigue and nausea were obsd. [276123]. The spectrum of activity of retigabine resembles that of valproate, but its potency is greater and toxicity is reduced [373379]. The mechanism of action of retigabine is probably multifactorial. Research has shown that retigabine acts as a selective K+ channel opener in neuronal cells and this can be expected to contribute to its anticonvulsant effect [273670]. In addn. it demonstrates potentiation of GABA transmission and possibly also weak modulation of sodium and calcium channels [299344]. Retigabine also has neuroprotective activity with potential for the treatment of stroke and neurodegenerative diseases, such as Alzheimer's disease, Huntington's disease and multiple sclerosis [249381]. In Feb. 2000, Lehman Brothers predicted product launch could be as early as 2002 for epilepsy in the US [357788]. In Feb. 1999, Lehman Brothers predicted that the first major launch date of the drug would be 2003, and the year of peak sales to be 2011 [319225].

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:31314 CAPLUS
DOCUMENT NUMBER: 134:80838
TITLE: New uses of retigabine and other potassium channel openers
INVENTOR(S): Burbidge, Stephen Anthony; Clare, Jeffrey John; Cox, Brian; Dupere, Joseph; Hagan, Russell Michael; Xie, Xinmin
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001001970	A2	20010111	WO 2000-GB2516	20000630
WO 2001001970	A3	20020228		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1207863	A2	20020529	EP 2000-940669	20000630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003503447	T2	20030128	JP 2001-507464	20000630

PRIORITY APPLN. INFO.: GB 1999-15414 A 19990701
WO 2000-GB2516 W 20000630

AB The present invention relates to therapeutic uses of KCNQ2/3 potassium channel openers, including retigabine, for treatment of various diseases, esp. epilepsy, in a mammal, including man. Besides being used as antiepileptics, KCNQ2/3 potassium channel openers may be used as muscle relaxants, fever reducers, anxiolytics, antimigraine agents, and analgesics, for treatment of bipolar disorders, unipolar depression, functional bowel disorders, or tinnitis, for preventing and reducing drug dependence or tolerance, for treatment of cancer, inflammation, ophthalmic diseases, and various CNS disorders. KCNQ2/3 potassium channel openers may be formulated in various dosage forms alone or in combination with one or more other therapeutic agents.

L5 ANSWER 26 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:24920 CAPLUS
DOCUMENT NUMBER: 134:231797
TITLE: Investigations into the mechanism of action of the new anticonvulsant retigabine: interaction with GABAergic and glutamatergic neurotransmission and with voltage gated ion channels
AUTHOR(S): Rundfeldt, Chris; Netzer, Rainer
CORPORATE SOURCE: Department of Pharmacology 1, Arzneimittelwerk Dresden GmbH, Corporate R&D, ASTA Medica Group, Radebeul, Germany
SOURCE: Arzneimittel-Forschung (2000), 50(12), 1063-1070
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retigabine (N-(2-amino-4-(4-fluorobenzylamino)phenyl) carbamic acid Et ester, CAS 150812-12- 7, D-23129) is a novel anticonvulsant currently undergoing phase II clin. trials. The compd. was shown to possess broad spectrum and potent anticonvulsant properties both in vitro and in vivo. The mechanism of action of this drug is currently not fully understood. In previous studies a potent opening effect on K- channels and an increased release of newly synthesized .gamma.-aminobutyric acid (GABA) were reported. The aim of this study was to investigate the interaction of retigabine with GABA, kainate and N-methyl-D-aspartate (NMDA) induced currents as well as with voltage gated Na+ and Ca++ channels. Retigabine concn. dependently potentiated GABA induced currents in rat cortical neurons. Significant effects were only seen with concns. of 10 .mu.mol/l and above. The action of retigabine was not antagonized by flumazenil indicating interaction with other than benzodiazepine binding sites. In comparison with the K+ channel opening effect which can be seen at concns. as low as 0.1 .mu.mol/l the contribution of this mechanism to the anticonvulsant activity of retigabine may be minor. Inhibitory effects obsd. on voltage activated Na+ and Ca++ channels as well as on kainate induced currents were only obsd. at the highest concn. tested (100 .mu.mol/l) and can be considered non specific. No significant interaction with NMDA induced currents was obsd.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 27 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:13247 CAPLUS
DOCUMENT NUMBER: 135:55944
TITLE: A neurochemical study of the novel antiepileptic drug retigabine in mouse brain
AUTHOR(S): Sills, Graeme J.; Rundfeldt, Chris; Butler, Elaine; Forrest, Gerard; Thompson, George G.; Brodie, Martin J.
CORPORATE SOURCE: Epilepsy Unit, University Department of Medicine and Therapeutics, Western Infirmary, Glasgow, G11 6NT, UK
SOURCE: Pharmacological Research (2000), 42(6), 553-557
CODEN: PHMREP; ISSN: 1043-6618

PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The novel antiepileptic drug, retigabine, was reported to have multiple mechanisms of action, including potentiation of .gamma.-aminobutyric acid (GABA) and glutamate synthesis. The authors have investigated its effects on several GABA- and Glu-related neurochem. parameters in mouse brain. Mice were administered retigabine either as a single dose or daily for 5 days. At 4 h after dosing, brains were removed and analyzed for GABA, Glu, and Gln concns. and for the activities of GABA-transaminase and Glu decarboxylase. Single doses of retigabine lowered brain concns. of Glu and Gln. Repeated treatment reduced the activity of GABA-transaminase. The drug was essentially without effect on all other parameters investigated. These results suggest that retigabine blocks GABA metab. rather than enhancing GABA synthesis. In addn., the drug may also lower brain concns. of the excitatory neurotransmitter Glu and its precursor, Gln. These effects may contribute to the antiepileptic action of retigabine. (c) 2000 The Italian Pharmacological Society.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 28 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:819672 CAPLUS
DOCUMENT NUMBER: 134:65759
TITLE: Determination of retigabine and its acetyl metabolite in biological matrices by on-line solid-phase extraction (column switching) liquid chromatography with tandem mass spectrometry
AUTHOR(S): Knebel, N. G.; Grieb, S.; Leisenheimer, S.; Locher, M.
CORPORATE SOURCE: Department of Biological Research Biochemistry, ASTA Medica AG, Frankfurt, 60314, Germany
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2000), 748(1), 97-111
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A HPLC assay with tandem mass spectrometric detection in the pos.-ion atm. pressure chem. ionisation (APCI) mode for the sensitive detn. of retigabine [(I), D-23129] and its acetyl metabolite [(II), ADW 21-360] in plasma was developed, utilizing the structural analog (D-10328), (III), as internal std. Automated online solid-phase extn. of dild. plasma samples, based on 200-.mu.l plasma aliquots, at pH 6.5, allowed a reliable quantification of retigabine and the acetyl metabolite down to 1 ng/mL. Injection of 500 .mu.l of dild. plasma onto a C2 stationary phase-based column switching system in combination with a 75 mm.times.4 mm reversed-phase anal. column at a flow-rate of 0.5 mL/min provided cycle times of 4 min per sample. The std. curves were linear from 1 to 1000 ng/mL using weighted linear regression anal. (1/x2). The method is accurate (mean accuracy .ltoreq..+-.10%), precise (RSD <.+-.15%) and sensitive, providing lower limits of quantification in plasma of 1 ng/mL for retigabine (I), and 2.5 ng/mL for the metabolite (II) with limits of detection of 0.5 ng/mL for both analytes. Up to 200 unknowns may be analyzed each 24 h per analyst.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 29 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:636213 CAPLUS
DOCUMENT NUMBER: 133:187979
TITLE: Use of retigabine for the treatment of pain
INVENTOR(S): Rundfeldt, Chris; Bartsch, Reni; Rostock, Angelika; Tober, Christine; Dost, Rita
PATENT ASSIGNEE(S): ASTA Medica Aktiengesellschaft, Germany

SOURCE: U.S., 5 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6117900	A	20000912	US 1999-406135	19990927
WO 2001022953	A2	20010405	WO 2000-EP9284	20000922
WO 2001022953	A3	20020523		
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
BR 2000014293	A	20020521	BR 2000-14293	20000922
EP 1223927	A2	20020724	EP 2000-969283	20000922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY				
NZ 517616	A	20021220	NZ 2000-517616	20000922
JP 2003510273	T2	20030318	JP 2001-526165	20000922
EE 200200145	A	20030415	EE 2002-145	20000922
BG 106450	A	20020930	BG 2002-106450	20020227
NO 2002001418	A	20020321	NO 2002-1418	20020321

PRIORITY APPLN. INFO.: US 1999-406135 A 19990927
WO 2000-EP9284 W 20000922

AB The invention relates to the use of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene (retigabine), or a pharmaceutically utilizable salt thereof, for the prophylaxis and treatment of pain, e.g. neuropathic pain.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 30 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:614970 CAPLUS
DOCUMENT NUMBER: 133:291018
TITLE: Retigabine, a novel anti-convulsant, enhances activation of KCNQ2/Q3 potassium channels
AUTHOR(S): Wickenden, Alan D.; Yu, Weifeng; Zou, Anrou; Jegla, Tim; Wagoner, P. Kay
CORPORATE SOURCE: ICAgen Inc., Durham, NC, USA
SOURCE: Molecular Pharmacology (2000), 58(3), 591-600
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retigabine [N-(2-amino-4-[fluorobenzylamino]-phenyl) carbamic acid; D-23129] is a novel anticonvulsant, unrelated to currently available antiepileptic agents, with activity in a broad range of seizure models. In the present study, we sought to det. whether retigabine could enhance current through M-like currents in PC12 cells and KCNQ2/Q3 K+ channels expressed in Chinese hamster ovary cells (CHO-KCNQ2/Q3). In differentiated PC12 cells, retigabine enhanced a linopirdine-sensitive current. The effect of retigabine was assocd. with a slowing of M-like tail current deactivation in these cells. Retigabine (0.1 to 10 .mu.M) induced a potassium current and hyperpolarized CHO cells expressing KCNQ2/Q3 cells but not in wild-type cells. Retigabine-induced currents in CHO-KCNQ2/Q3 cells were inhibited by 60.6 .+-. 11% (n = 4) by the KCNQ2/Q3 blocker, linopirdine (10 .mu.M), and 82.7 .+-. 5.4% (n = 4) by BaCl2 (10 mM). The mechanism by which retigabine enhanced KCNQ2/Q3 currents involved large, drug-induced, leftward shifts in the voltage dependence of

channel activation (-33.1 .+-. 2.6 mV, n = 4, by 10 .mu.M retigabine). Retigabine shifted the voltage dependence of channel activation with an EC50 value of 1.6 .+-. 0.3 .mu.M (slope factor was 1.2 .+-. 0.1, n = 4 to 5 cells per concn.). Retigabine (0.1 to 10 .mu.M) also slowed the rate of channel deactivation, predominantly by increasing the contribution of a slowly deactivating tail current component. Our findings identify KCNQ2/Q3 channels as a mol. target for retigabine and suggest that activation of KCNQ2/Q3 channels may be responsible for at least some of the anticonvulsant activity of this agent.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 31 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:548515 CAPLUS

DOCUMENT NUMBER: 133:232694

TITLE: Modulation of KCNQ2/3 potassium channels by the novel anticonvulsant retigabine

AUTHOR(S): Main, Martin J.; Cryan, Jennifer E.; Dupere, Joe R. B.; Cox, Brian; Clare, Jeffrey J.; Burbidge, Stephen A.

CORPORATE SOURCE: Molecular Pharmacology, Unit, Glaxo-Wellcome Research and Development, Stevenage, UK

SOURCE: Molecular Pharmacology (2000), 58(2), 253-262 CODEN: MOPMA3; ISSN: 0026-895X

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Retigabine is a novel anticonvulsant with an unknown mechanism of action. It has recently been reported that retigabine modulates a potassium channel current in nerve growth factor-differentiated PC12 cells, however, to date the mol. correlate of this current has not been identified. In the present study we have examd. the effects of retigabine on recombinant human KCNQ2 and KCNQ3 potassium channels, expressed either alone or in combination in Xenopus oocytes. Application of 10 .mu.M retigabine to oocytes expressing the KCNQ2/3 heteromeric channel shifted both the activation threshold and voltage for half-activation by approx. 20 mV in the hyperpolarizing direction, leading to an increase in current amplitude at test potentials between -80 mV and +20 mV. Retigabine also had a marked effect on KCNQ current kinetics, increasing the rate of channel activation but slowing deactivation at a given test potential. Similar effects of retigabine were obsd. in oocytes expressing KCNQ2 alone, suggesting that KCNQ2 may be the mol. target of retigabine. Membrane potential recordings in oocytes expressing the KCNQ2/3 heteromeric channel showed that application of retigabine leads to a concn.-dependent hyperpolarization of the oocyte, from a resting potential of -63 mV under control conditions to -85 mV in the presence of 100 .mu.M retigabine (IC50 = 5.2 .mu.M). In control expts. retigabine had no effect on either resting membrane potential or endogenous oocyte membrane currents. In conclusion, we have shown that retigabine acts as a KCNQ potassium channel opener. Because the heteromeric KCNQ2/3 channel has recently been reported to underlie the M-current, it is likely that M-current modulation can explain the anticonvulsant actions of retigabine in animal models of epilepsy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 32 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:490598 CAPLUS

DOCUMENT NUMBER: 133:217641

TITLE: Flupirtine and retigabine prevent l-glutamate toxicity in rat pheochromocytoma PC 12 cells

AUTHOR(S): Seyfried, J.; Evert, B. O.; Rundfeldt, C.; Schulz, J. B.; Kovar, K. A.; Klockgether, T.; Wullner, U.

CORPORATE SOURCE: Department of Neurology, University of Tubingen, Tubingen, D-72076, Germany
SOURCE: European Journal of Pharmacology (2000), 400(2/3), 155-166
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Flupirtine is an analgesic drug thought to have NMDA receptor antagonistic and antiapoptotic effects. We investigated the effects of Ethyl-2-amino-6-(4-(4-fluorbenzyl)amino)-pyridine-3-carbamamic acid, maleate (flupirtine) and the related compd. N-(2-amino-4-(4-fluorobenzylamino)-phenyl)-carbamic acid, Et ester (retigabine) (Desaza-flupirtine) on the toxicity of l-glutamate and l-3,4-dihydroxyphenylalanine (l-DOPA) in rat pheochromocytoma PC 12 cells in vitro. Both drugs (10 .mu.M) markedly decreased nonreceptor-mediated necrotic cell death in PC 12 cultures treated with l-glutamate (10 mM) for 72 h. In contrast, apoptosis induced by l-DOPA (250 .mu.M) after 48 h was not affected by either substance. While l-DOPA elicited massive generation of reactive oxygen intermediates, l-glutamate-induced cell death was accompanied by only slightly increased levels of reactive oxygen intermediates. Flupirtine and retigabine exerted anti-oxidative effects in PC 12 cultures independent of their ability to prevent cell death. Further examn. of the protective action of flupirtine and retigabine against l-glutamate toxicity showed that it had no influence on monoamine oxidase (monoamine: oxygen oxidoreductase (deaminating), EC 1.4.3.4., MAO) activity. Thus, flupirtine and retigabine provided protection against cystine deprivation and l-glutamate toxicity but did not protect against l-glutamate under cystine-free conditions indicating that both compds. are sufficiently effective to compensate the oxidative stress elicited by cystine deprivation but not excessive activity of monoamine oxidase after l-glutamate treatment.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 33 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:155814 CAPLUS
DOCUMENT NUMBER: 133:621
TITLE: The novel anticonvulsant retigabine activates M-currents in Chinese hamster ovary-cells transfected with human KCNQ2/3 subunits
AUTHOR(S): Rundfeldt, C.; Netzer, R.
CORPORATE SOURCE: ASTA Medica Group, Corporate R&D, Department of Pharmacology, Arzneimittelwerk Dresden GmbH, Radebeul, D-01445, Germany
SOURCE: Neuroscience Letters (2000), 282(1,2), 73-76
CODEN: NELED5; ISSN: 0304-3940
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retigabine (D-23129) is a novel antiepileptic compd. with broad spectrum and potent anticonvulsant properties, both in vitro and in vivo. The compd. was shown to activate a K+ current in neuronal cells. The pharmacol. of the induced current displays concordance with the published pharmacol. of the M-channel, which recently was correlated to the KCNQ2/3 K+ channel heteromultimere. We examd. the effect of retigabine on KCNQ2/3 expressed in Chinese hamster ovary cells. The compd. concn.-dependently activated a K+ current in transfected cells clamped at -50 mV. The activation was induced by a shift of the opening threshold to more neg. potentials. The effect was not mediated by an interaction with the cAMP modulatory site and could be partially blocked by the M-channel antagonist linopirdine. The data display that retigabine is the first described M-channel agonist and support the hypothesis that M-channel agonism is a new mode of action for anticonvulsant drugs. Since the function of this

channel is reduced in a hereditary epilepsy syndrome, retigabine may be the first anticonvulsant to directly target the deficit obsd. in a channelopathy.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:92840 CAPLUS
DOCUMENT NUMBER: 133:12647
TITLE: Effects of retigabine (D-23129) on different patterns of epileptiform activity induced by low magnesium in rat entorhinal cortex hippocampal slices
AUTHOR(S): Armand, V.; Rundfeldt, C.; Heinemann, U.
CORPORATE SOURCE: Department of Neurophysiology, Institute of Physiology, Universitatsklinikum Charite, Humboldt University Berlin, Berlin, D 10117, Germany
SOURCE: Epilepsia (2000), 41(1), 28-33
CODEN: EPILAK; ISSN: 0013-9580
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study evaluated the effect of a new antiseizure drug, retigabine (D-23129; N-(2-amino-4-[fluorobenzylamino]phenyl)carbamic acid Et ester) on low-Mg2+-induced epileptiform discharges in vitro. Three types of epileptiform discharges (recurrent short discharges in the hippocampus, seizure-like events, and late recurrent discharges in the entorhinal cortex [EC]) were elicited in rat EC-hippocampal slices by perfusion with low-Mg2+-artificial cerebrospinal fluid. The antiepileptic properties of retigabine were evaluated as effect on the frequency and amplitude of the epileptiform activities as well as on the time of onset of the effect in the EC and in hippocampal area CA1 by using extracellular recording techniques. Retigabine at 20 .mu.M reversibly suppressed the recurrent short discharges in CA1 otherwise sensitive only to high concns. of valproate but insensitive to std. antiepileptic drugs (AEDs), whereas 10 .mu.M reduced the frequency of discharges by 34%, with no significant effect on the amplitude. In the EC, 50 .mu.M retigabine reversibly suppressed the seizure-like events, whereas 20 .mu.M blocked seizure-like events in 71.5% of the slices. The seizure-like events were also sensitive to std. AEDs. Late recurrent discharges in the EC that were not blocked by std. AEDs were reversibly suppressed by 100 .mu.M retigabine, whereas 50 .mu.M reduced the frequency of the discharges by 94.4%, and 20 .mu.M by 74.2%, with no effect on the amplitude. Retigabine is an effective AED with suppressive effects on recurrent short discharges and on late recurrent discharges normally insensitive to std. AEDs.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 35 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:24763 CAPLUS
DOCUMENT NUMBER: 132:175705
TITLE: The anticonvulsant retigabine potently suppresses epileptiform discharges in the low Ca++ and low Mg++ model in the hippocampal slice preparation
AUTHOR(S): Dost, R.; Rundfeldt, C.
CORPORATE SOURCE: Dep. Pharmacol., ASTA Medica Group, Arzneimittelwerk Dresden GmbH, Corporate R&D, Radebeul, D-01445, Germany
SOURCE: Epilepsy Research (2000), 38(1), 53-66
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retigabine (N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid Et ester, D-23129) is a broad acting anticonvulsant currently undergoing

phase II clin. trials. An opening effect on leakage conductance K+ channels, potential of GABA induced currents and a weak blocking effect on Na+ and Ca++ channels were previously reported. The goal of this study was to investigate whether retigabine is capable of blocking epileptiform discharges in the low Ca++ and low Mg++ model in the hippocampal slice prepns. and whether the anti-burst activity can be related to the K+ channel opening effect. In the low Ca++ model, synaptic transmission is blocked and discharges evolve from ephaptically-coupled neurons. Compds. which directly interfere with the threshold for action potential induction via alteration of ion channel function (i.e. Na+ channel blocker) may later the discharges, while compds. interfering with synaptic transmission are not active. Retigabine suppressed the discharges in a concn.-dependent manner. A significant redn. in frequency without effect on amplitude was obsd. after application of 1 .mu.M, and a full block of all discharges after application of 25 .mu.M. The opener of the ATP-sensitive K+ channels cromakalim was also active. Application of 300 .mu.M cromakalim yielded to a lower frequency with no effects on the amplitude of discharges. Treatment with phenytoin and carbamazepine resulted in a marked redn. in amplitude accompanied by a rise in frequency; only at higher concns. was a full block obsd. The effect of retigabine therefore differs from sodium channel blockers and can be related to the K+ channel opening effect. In the low Mg++ model, excitatory neurotransmission is augmented by reducing the Mg++ block of NMDA channels. This results in development of interictal-like epileptiform activity in area CA1 in isolated hippocampal slices. Treatment with retigabine 10 .mu.M resulted in a significant redn. of the discharges, and discharges were fully blocked after application of 25 .mu.M. Qual. similar effects were obsd. with cromakalim and valproate, albeit at higher concns. The data indicate that retigabine exerts potent broad spectrum activity making it an interesting candidate for treatment of drug resistant patients.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 36 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:8336 CAPLUS

DOCUMENT NUMBER: 132:161138

TITLE: Retigabine strongly reduces repetitive firing in rat entorhinal cortex

AUTHOR(S): Hetka, R.; Rundfeldt, C.; Heinemann, U.; Schmitz, D.

CORPORATE SOURCE: Corporate R&D, Department of Pharmacology, Arzneimittelwerk Dresden, ASTA Medica Group, Radebeul, D-01445, Germany

SOURCE: European Journal of Pharmacology (1999), 386(2/3), 165-171
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Retigabine (D-23129) [N-(2-amino-4-(4-fluorobenzylamino)phenyl)carbamic acid Et ester] is a novel antiepileptic drug. The compd. was shown to possess anticonvulsant properties both in vivo and in vitro. We investigated the effects of retigabine on neurons in the rat medial entorhinal cortex using conventional intracellular recordings in combined hippocampal-entorhinal cortex slices. Retigabine strongly reduced the no. of action potentials elicited by 1 s long depolarizing current injections. Both the amplitudes of monosynaptic inhibitory postsynaptic potentials/currents (IPSP/Cs) and the amplitudes of excitatory postsynaptic potentials (EPSPs) remained unaffected. The drug increased outward rectification and induced a membrane-potential hyperpolarization in most of the tested neurons. The findings suggest that retigabine exerts its anticonvulsant effects by activation of a K+-conductance, however it cannot be excluded from our expts. that other mechanisms may be involved in the effect of retigabine on membrane properties.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 37 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:305307 CAPLUS
DOCUMENT NUMBER: 131:128233
TITLE: Potassium channels and neurodegenerative diseases
AUTHOR(S): Rundfeldt, Chris
CORPORATE SOURCE: Dept. of Pharmacology I, Corporate R and D, ASTA Medica GmbH, Radebeul, D-01445, Germany
SOURCE: Drug News & Perspectives (1999), 12(2), 99-104
CODEN: DNPEED; ISSN: 0214-0934
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 43 refs. Many different insults and mechanisms can lead to neurodegeneration. Potassium channel openers may play a role in counteracting or preventing this damage. A heterogeneous array of potassium channels, classified according to their electrophysiol. properties, has been identified. Different potassium channels are involved in several steps within the pathophysiol. cascade that ultimately leads to cell death; therefore, several potassium channel openers may interfere with different steps within the neurodegenerative cascade. However, it is possible that in case of severe insults potassium channel opening may not lead to neuroprotection, due to the fact that potassium channels are already endogenously activated and the extracellular potassium concn. is already very high. Thus, further channel opening may have no addnl. pos. effects. Selective drugs for individual channel subtypes should be used in predictive models of neurodegeneration; however, the currently known potassium channel openers are few and nonselective. The classes of drugs that need to be explored include potassium channel openers of the ATP-sensitive, high-conductance calcium-sensitive, and inward rectifier or leakage types. Selective openers for inward rectifier potassium channels are currently not available, although activation of 5-HT1A receptors results in the induction of an inwardly rectifying potassium current. Potent neuroprotective properties have been described for different 5-HT1A agonists in models of focal and global ischemia. Retigabine, a leakage-current potassium channel opener, has been shown to have neuroprotective effects in animal models of neurodegeneration. Of the currently available potassium channel openers, retigabine and BAY-X-3702 are active at nontoxic doses. Further research is needed to develop selective, well-tolerated potassium channel openers.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 38 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:302440 CAPLUS
DOCUMENT NUMBER: 131:82548
TITLE: Metabolism of retigabine (D-23129), a novel anticonvulsant
AUTHOR(S): Hempel, Roland; Schupke, Hubert; Mcneilly, Patrick J.; Heinecke, Kristina; Kronbach, Christiane; Grunwald, Christian; Zimmermann, Gottfried; Griesinger, Christian; Engel, Jurgen; Kronbach, Thomas
CORPORATE SOURCE: Corporate Research and Development ASTA Medica Group, Radebeul, D-01445, Germany
SOURCE: Drug Metabolism and Disposition (1999), 27(5), 613-622
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retigabine (D-23129, N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic

acid Et ester) is a potent anticonvulsant in a variety of animal models. Rats metabolized [14C]retigabine mainly through glucuronidation and acetylation reactions. Glucuronides were detected in incubates with liver microsomes or slices, in plasma, and in bile and feces but were absent in urine (0-24 h) that contained about 2% of the dose as retigabine and approx. 29% of the dose in > 20 metabolites, which are derived mainly from acetylation reactions. About 67% of the radioactivity was excreted into feces, approx. 10% of the dose as glucuronide. The metabolite pattern in the urine (0-24 h) of dogs was comparatively simple in that retigabine (13%), retigabine-N-glucuronide (5%), and retigabine-N-glucoside (1%) were present. In the same 24-h interval, about 39% of unchanged retigabine was excreted into feces. Plasma profiling and spectroscopic anal. (liq. chromatog. with tandem mass spectrometry NMR) of two isolated urinary metabolites obtained after single oral dosing of 600 mg retigabine in healthy volunteers indicated that both acetylation and glucuronidation are major metabolic pathways of retigabine in humans. We found that in vitro assays with liver slices from rat and humans reveal the major circulating metabolites in vivo.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 39 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:302439 CAPLUS

DOCUMENT NUMBER: 131:82547

TITLE: Retigabine N-glucuronidation and its potential role in enterohepatic circulation

AUTHOR(S): Hiller, Anita; Nguyen, Nghia; Strassburg, Christian P.; Li, Qing; Jainta, Harald; Pechstein, Birgit; Ruus, Peter; Engel, Jurgen; Tukey, Robert H.; Kronbach, Thomas

CORPORATE SOURCE: Corporate Research and Development ASTA Medica Group, Radebeul, D-01445, Germany

SOURCE: Drug Metabolism and Disposition (1999), 27(5), 605-612 CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The metab. of retigabine in humans and dogs is dominated by N-glucuronidation (McNeilly et al., 1997), whereas in rats, a multitude of metabolites of this new anticonvulsant is obsd. (Hempel et al., 1999). The comparison of the in vivo and in vitro kinetics of retigabine N-glucuronidation in these species identified a const. ratio between retigabine and retigabine N-glucuronide in vivo in humans and dog. An enterohepatic circulation of retigabine in these species is likely to be the result of reversible glucuronidation-deglucuronidation reactions. Rats did not show such a phenomenon, indicating that enterohepatic circulation of retigabine via retigabine N-glucuronide does not occur in this species. In the rat, 90% of retigabine N-glucuronidation is catalyzed by UDP-glucuronosyltransferase (UGT)1A1 and UGT1A2, whereas family 2 UGT enzymes contribute also. Of ten recombinant human UGTs, only UGTs 1A1, 1A3, 1A4, and 1A9 catalyzed the N-glucuronidation of retigabine. From the known substrate specificities of UGT1A4 toward lamotrigine and bilirubin and our activity and inhibition data, we conclude that UGT1A4 is a major retigabine N-glucuronosyl transferase in vivo and significantly contributes to the enterohepatic cycling of the drug.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 40 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:263137 CAPLUS

DOCUMENT NUMBER: 131:179660

TITLE: Characterization of the K+ channel opening effect of the anticonvulsant retigabine in PC12 cells

AUTHOR(S): Rundfeldt, Chris
CORPORATE SOURCE: ASTA Medica Group, Corporate R&D, Department of Pharmacology, Arzneimittelwerk Dresden GmbH, Radebeul, D-01445, Germany
SOURCE: Epilepsy Research (1999), 35(2), 99-107
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Retigabine (D-23129) is a new anticonvulsant compd. which acts as a K+ channel opener in neuronal cells. The aim of the present study was to further characterize the retigabine induced K+ current. In nerve growth factor treated PC12 cells and in rat cortical neurons the application of retigabine activated a K+ current. In contrast, however, no K+ current activation was obsd. in untreated PC12 and in glial cells which were cultivated together with the neuronal cells. To characterize the retigabine activated K+ current, K+ channel blockers were used. The retigabine induced current was not affected by 1 and 10 mM 4-aminopyridine (4AP). Ba2+ 1 mM resulted in a redn. of 88.6.+-.3.0% (n=5); 10 mM abolished the current. Tetraethylammonium (TEA), 1 and 10 mM, reduced the current by 23.6.+-.3.1 and 61.6.+-.3.7%, resp. To investigate the current/voltage (I/V) relation of the current initiated by retigabine (10 .mu.M), cells were clamped to a holding potential of -80 mV and a ramp stimulation protocol (-120 to +60 mV in 5 s) was applied prior to and during application of retigabine. Subtraction of the two traces yielded the current induced by retigabine. A nearly linear relationship was detd. between -120 and -40 mV. At potentials pos. to -40 mV, the response was variable. This was due to the addnl. obsd. weak blocking effect of retigabine on delayed rectifier (Kdr) currents. If the ramp was applied in the presence of 10 mM 4AP to block Kdr, a nearly linear I/V-relationship was present from -120 to +60 mV. The comparison of the I/V relation and pharmacol. with published K+ channel subtypes gives evidence that an unknown neuronal K+ channel subtype may be involved.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 41 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:807142 CAPLUS
DOCUMENT NUMBER: 130:57310
TITLE: Structure and physicochemical properties of N-[2-amino-4-(4-fluorobenzylamino)-phenyl]ethylcarbamate, retigabine
AUTHOR(S): Thiel, W.
CORPORATE SOURCE: Arzneimittelwerk Dresden G.m.b.H., Radebeul, D-01445, Germany
SOURCE: Pharmazie (1998), 53(12), 865-869
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The structure of the anticonvulsant substance N-[2-amino-4-(4-fluorobenzylamino)-phenyl]ethylcarbamate (INN: retigabine) was proved by IR, UV, 1H NMR, 13C NMR and mass spectra. Retigabine is practically insol. in a neutral aq. medium at 20 .degree. (S .apprx. 0.07 g/l). The soly. of the substance in 0.1 N HCl is about 16 g/l. In DMF, retigabine is freely sol. (S .apprx. 186 g/l). The pK-value is about 3.7. The partition coeff. P = Coctanol/CWater at 37 .degree. ranging from 0.4 at pH .apprx. 1 to about 150 at pH .gtoreq. 5.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 42 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:792703 CAPLUS
DOCUMENT NUMBER: 130:261905

TITLE: Effects of retigabine (D-23129) on different patterns of epileptiform activity induced by 4-aminopyridine in rat entorhinal cortex hippocampal slices
AUTHOR(S): Armand, V.; Rundfeldt, C.; Heinemann, U.
CORPORATE SOURCE: Universitatklinikum Charite, Institute of Physiology, Department of Neurophysiology, Humboldt University Berlin, Tucholskystrasse 2, Berlin, D-10117, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1999), 359(1), 33-39
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to evaluate the effects of the new anticonvulsant drug N-(2-amino-4-[fluorobenzylamino]-phenyl) carbamic acid Et ester (retigabine, D-23129, ASTA Medica, Dresden, Germany) on different patterns of epileptiform activity induced by 4-aminopyridine (4AP) in rat entorhinal cortex hippocampal slices. Application of 4AP (100 mM) induced in entorhinal cortex two different types of epileptiform activities; seizure-like events (SLE) and interictal epileptiform discharges (IED). Bicuculline (10 mM) changed 4AP-induced SLE and IED to recurrent epileptiform discharges (RED). IED were isolated after blockade of the SLE by glutamate receptor antagonists for .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) and N-methyl-d-aspartate (NMDA) receptors, i.e. 1,2,3,4 tetrahydro-6-nitro-2,3-dioxo-benzo[f]quinoxaline-7-sulfonamide (NBQX, 10 mM) and 2-amino-5-phosphonovaleric acid (APV, 30 mM). Anticonvulsant properties of retigabine were evaluated as effect on the frequency and amplitude of SLE, IED and RED. Retigabine suppressed all types of epileptiform events in a dose dependent and reversible manner. SLE were suppressed in 71.4 and 100% of slices by 5 and 10 mM, resp. The frequency of IED was significantly reduced by 20 mM retigabine (40.9.+-.24.5%) and IED were blocked completely by 50 mM retigabine. When IED were isolated by application of glutamate antagonists 20 mM retigabine was sufficient to block this activity completely. RED induced by combined application of bicuculline and 4AP were blocked in 71.4% of the tested slices with 100 mM retigabine. The frequency of the RED in the remaining slices was reduced by 96.1.+-.6.1%. We conclude that retigabine acts on a large variety of different epileptiform activities in temporal lobe structures that are known to develop readily pharmacoresistant seizures.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 43 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:646571 CAPLUS
DOCUMENT NUMBER: 127:326363
TITLE: The new anticonvulsant retigabine (D-23129) acts as an opener of K+ channels in neuronal cells
AUTHOR(S): Rundfeldt, Chris
CORPORATE SOURCE: Department of Pharmacology, Arzneimittelwerk Dresden GmbH, Corporate R and D, ASTA Medica Group, Meissner Strasse 35, Radebeul, D-01445, Germany
SOURCE: European Journal of Pharmacology (1997), 336(2/3), 243-249
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The patch-clamp technique was used to measure currents passing through K+ channels in neuronal cell prepns. Retigabine (D-23129, N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid Et ester) activated a K+ conductance in slightly depolarized NG108-15 neuronal cells in a dose-dependent manner (0.1-10 .mu.M). At the K+ reversal potential, no current could be elicited and in hyperpolarized cells the current was reversed. A similar current was elicited in primary cultures of mouse

cortical neurons and in differentiated hNT cells, a cell line derived from human neuronal cells. At higher concns., retigabine also partially blocked voltage activated K+ currents. None of the tested anticonvulsants, phenytoin, carbamazepine and valproate and none of the K+ channel openers cromakalim, diazoxide and pinacidil exerted a similar effect. The current was not affected by the K+ channel blocker glibenclamide (10 .mu.M) but was fully blocked by application of Ba2+ (10.8 mM). Exchange of K+ with cesium in the intracellular space also fully abolished the current. It can be expected that the K+ channel opening effect contributes to the anticonvulsant activity of retigabine.

L5 ANSWER 44 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:377765 CAPLUS
DOCUMENT NUMBER: 126:338857
TITLE: Use of 4-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene for prevention and treatment of sequelae of poor cerebral circulation or neurodegenerative diseases
INVENTOR(S): Rostock, Angelika; Tober, Christine; Rundfeldt, Chris; Bartsch, Reni
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19539861	A1	19970430	DE 1995-19539861	19951026
WO 9715300	A2	19970501	WO 1996-DE1951	19961015
WO 9715300	A3	19970703		
W: AU, BR, BY, CA, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SK, UA				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9715400	A1	19970515	AU 1997-15400	19961015
AU 706735	B2	19990624		
EP 857065	A2	19980812	EP 1996-945354	19961015
EP 857065	B1	19990407		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 178487	E	19990415	AT 1996-945354	19961015
BR 9610899	A	19990713	BR 1996-10899	19961015
ES 2131973	T3	19990801	ES 1996-945354	19961015
JP 11515007	T2	19991221	JP 1996-516185	19961015
NZ 326754	A	20000327	NZ 1996-326754	19961015
IL 123523	A1	20011223	IL 1996-123523	19961015
SK 283222	B6	20030304	SK 1998-520	19961015
CZ 291456	B6	20030312	CZ 1998-1225	19961015
RU 2201227	C2	20030327	RU 1998-109951	19961015
TW 457084	B	20011001	TW 1996-85112851	19961021
CA 2188841	AA	19970427	CA 1996-2188841	19961025
ZA 9608991	A	19970610	ZA 1996-8991	19961025
US 5852053	A	19981222	US 1996-736166	19961028
US 5849789	A	19981215	US 1997-937420	19970925
NO 9801503	A	19980402	NO 1998-1503	19980402

PRIORITY APPLN. INFO.: DE 1995-19539861 A 19951026
WO 1996-DE1951 W 19961015
US 1996-736166 A3 19961028

AB The title compd. (I) and its salts are useful as neuroprotectants for prevention and treatment of stroke, impaired cerebral circulation, and neurodegenerative diseases. Thus, a learning deficit in rats with a ligated carotid artery was reversed by administration of I (2 mg/kg i.p.).

L5 ANSWER 45 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:357310 CAPLUS
DOCUMENT NUMBER: 127:75470
TITLE: In vitro glucuronidation of D-23129, a new anticonvulsant, by human liver microsomes and liver slices
AUTHOR(S): McNeilly, P. J.; Torchin, C. D.; Anderson, L. W.; Kapetanovic, I. M.; Kupferberg, H. J.; Strong, J. M.
CORPORATE SOURCE: Laboratory Clinical Pharmacology, Office Pharmaceutical Sciences, Center Drug Evaluation Research, US Food Drug Administration, Laurel, MD, 20708, USA
SOURCE: Xenobiotica (1997), 27(5), 431-441
CODEN: XENOBH; ISSN: 0049-8254
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The metabolic profile of D-23129, a new anticonvulsant agent, was studied in vitro using human liver microsomes and fresh liver slices. Oxidative metab. appeared to be minimal with D-23129. The percent mean total radioactivity not assocd. with the parent compd. recovered from oxidative metab. studies from three individual liver donors was 0.cntdot.7%.+-.0.cntdot.6 SD and was not significantly different from [14C]-D-23129 incubated with heat inactivated microsomes, mean = 0.cntdot.5%.+-.0.cntdot.4 SD. Phase II conjugation dominated the metab. of D-23129 producing two distinct N-glucuronides as the primary metabolites. These metabolites were identified by electrospray ionization LC/MS. The apparent Km for one of the glucuronide metabolites was detd. in human liver microsome prepns. from two individual liver donors to be 131 and 264 .mu.M resp. Vmax detd. for the same microsomal prepns. yielded 48.cntdot.9 and 59.cntdot.p pmol/min/mg protein.

L5 ANSWER 46 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:749838 CAPLUS
DOCUMENT NUMBER: 126:26281
TITLE: D-23129: A new anticonvulsant compound
AUTHOR(S): Kapetanovic, Izet M.; Rundfeldt, Chris
CORPORATE SOURCE: National Institute Neurological Disorders and Stroke, National Institutes Health, Bethesda, MD, USA
SOURCE: CNS Drug Reviews (1996), 2(3), 308-321
CODEN: CDREFB; ISSN: 1080-563X
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 42 refs., of the chem., pharmacokinetics, and clin. pharmacol. of D-23129 as a new anticonvulsant.

L5 ANSWER 47 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:374503 CAPLUS
DOCUMENT NUMBER: 125:104861
TITLE: D-23129: A new anticonvulsant with a broad spectrum activity in animal models of epileptic seizures
AUTHOR(S): Rostock, Angelika; Tober, Christine; Rundfeldt, Chris; Bartsch, Reni; Engel, Juergen; Polymeropoulos, Emanuele E.; Kutscher, Bernhard; Loescher, Wolfgang; Hoenack, Dagmar; et al.
CORPORATE SOURCE: ASTA Medica Group, Department Pharmacology, Radebeul, D-01445, Germany
SOURCE: Epilepsy Research (1996), 23(3), 211-223
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anticonvulsant activity of the novel drug D-23129 (N-(2-amino-4-(4-

fluorobenzylamino)phenyl)carbamic acid Et ester) was evaluated in animal models of epileptic seizures. D-23129 was active after oral and i.p. administration in rats and mice in a range of anticonvulsant tests at nontoxic doses. The compd. was active against elec. induced seizures (MES, ED50 rat p.o. = 2.87 mg/kg), against seizures induced chem. by pentylenetetrazole (s.c. PTZ, ED50 mouse p.o. = 13.5 mg/kg), picrotoxin and N-methyl-D-aspartate (NMDA) and in a genetic animal model, the DBA/2 mouse. It was not active against seizures induced by bicuculline and strychnine. Motor impairment, evaluated with the rotarod test and by observation in the open field, was minimal at doses showing anticonvulsant activity. D-23129 was very effective in elevating the threshold for elec. and chem. induced seizures. Considering the dose increasing the MES threshold by 50% (TID50 mouse i.p. = 1.6 mg/kg; TID50 rat i.p. = 0.72 mg/kg) and the TD50 obtained in the rotarod test, the protective index of D-23129 is better than that of valproate and phenytoin. During 14 days chronic oral treatment with 15 mg/kg, no development of tolerance was obsd. D-23129 thus presents an orally active, safe, broad spectrum anticonvulsant agent, which is structurally unrelated to anticonvulsants currently used. We expect that D-23129 will improve the treatment of refractory seizures in humans.

L5 ANSWER 48 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:347688 CAPLUS
DOCUMENT NUMBER: 125:76080
TITLE: D-23129: a potent anticonvulsant in the amygdala kindling model of complex partial seizures
AUTHOR(S): Tober, Christine; Rostock, Angelika; Rundfeldt, Chris; Bartsch, Reni
CORPORATE SOURCE: Department of Pharmacology, Corporate Research and Development, ASTA Medica Group, Arzneimittelwerk Dresden, Meissner Strasse 191, D-01445, Radebeul, Germany
SOURCE: European Journal of Pharmacology (1996), 303(3), 163-169
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The novel anticonvulsant drug D-23129 (N-(2-amino-4-(4-fluorobenzylamino)-phenyl) carbamic acid Et ester) was evaluated in the amygdala kindling model of complex partial seizures in rats. D-23129 exerts potent anticonvulsant activity against both focal and generalized seizures in animal models of epilepsy. After i.p. and oral administration in kindled rats, the substance dose dependently increased the threshold for induction of afterdischarges, exerting significant effects already after 0.01 mg/kg. In higher doses (2.5-5 mg/kg i.p., 10-15 mg/kg p.o.) D-23129 also exerted anticonvulsant effects on other seizure parameters of amygdala-kindled rats, i.e. seizure severity, seizure duration, total duration of behavioral changes and afterdischarge duration. The adverse effects of D-23129 were quantitated in the open field and in the rotarod test, a std. test for motor impairment. D-23129 exerted no adverse effects on behavior in doses up to 5 mg/kg i.p. and 15 mg/kg p.o. Comparing the adverse effects between kindled and non-kindled rats, no differences were found. The data demonstrate that D-23129 is more potent in the amygdala kindling model of complex partial seizures than in other seizure models. D-23129 is orally active and is devoid of neurotoxic effects in anticonvulsant doses, thus indicating that this compd. has potential for antiepileptic therapy.

L5 ANSWER 49 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:93161 CAPLUS
DOCUMENT NUMBER: 124:194122
TITLE: The effects of D-23129, a new experimental anticonvulsant drug, on neurotransmitter amino acids

in the rat hippocampus in vitro
AUTHOR(S): Kapetanovic, Izet M.; Yonekawa, Wayne D.; Kupferberg, Harvey J.
CORPORATE SOURCE: National Institute Neurological Disorders and Stroke, National Institutes Health, Bethesda, MD, 20892, USA
SOURCE: Epilepsy Research (1995), 22(3), 167-73
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB D-23129 [N-(2-amino-4-(4-fluorobenzylamino)phenyl)carbamic acid Et ester] and D-20443 (dihydrochloride of D-23129) are promising anticonvulsant compds. with a broad spectrum activity in animal models of epilepsy. Their effects on de novo synthesis of excitatory (glutamate and aspartate) and inhibitory (GABA) amino acids were studied in rat hippocampal slices. Like phenytoin, carbamazepine, lamotrigine, losigamone, U54494A, and flupirtine, D-23129 and D-20443 were effective in preventing the effects of a chemoconvulsant, 4-aminopyridine, on de novo synthesis of the three amino acids. However, unlike the other compds., D-23129 and D-20443 also preferentially increased the concns. of newly synthesized GABA. Their effect on the neosynthesis of GABA was unique, dose dependent, and not tetrodotoxin sensitive. A total of 15 compds. (including std., new and candidate anticonvulsants) either had no effect on new GABA or decreased it. Therefore, D-23129 and D-20443 exhibited two different effects on de novo synthesis of neurotransmitter amino acids, both of which could potentially be anticonvulsant in nature.

L5 ANSWER 50 OF 59 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:625705 CAPLUS
DOCUMENT NUMBER: 119:225705
TITLE: 1,2,4-triaminobenzene derivatives and a process for their preparation
INVENTOR(S): Dieter, Hans Reinhold; Engel, Juergen; Kutscher, Bernhard; Polymeropoulos, Emmanuel; Szelenyi, Stefan; Nickel, Bernd
PATENT ASSIGNEE(S): Asta Medica AG, Germany
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4200259	A1	19930715	DE 1992-4200259	19920108
EP 554543	A2	19930811	EP 1992-121028	19921210
EP 554543	A3	19931027		
EP 554543	B1	19960228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 134611	E	19960315	AT 1992-121028	19921210
ES 2084914	T3	19960516	ES 1992-121028	19921210
CA 2086654	AA	19930709	CA 1993-2086654	19930104
ZA 9300011	A	19930805	ZA 1993-11	19930104
JP 05345752	A2	19931227	JP 1993-1054	19930107
JP 3145220	B2	20010312		
US 5384330	A	19950124	US 1993-2458	19930108

PRIORITY APPLN. INFO.: DE 1992-4200259 A 19920108
OTHER SOURCE(S): CASREACT 119:225705; MARPAT 119:225705
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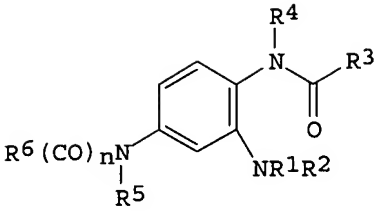

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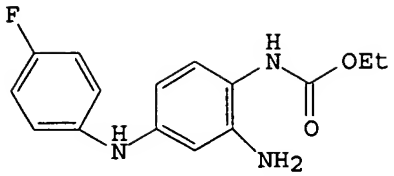

II

AB The title compds., 2-amino-1,4-bis(acylamino)benzene derivs. I (R1 = hydrogen, alkyl, etc.; R3 = alkoxy, amino, etc.; R4, R5 = hydrogen, alkyl; R6 = arylalkyl) and pharmaceuticals contg. them are claimed. I are anticonvulsants, antipyretics, antiepileptics, muscle relaxants, and peripheral analgesics. Some I were tested as antiepileptics in electroshock-induced convulsions in rats. Reductive carbamoylation of 2-amino-4-[(4-fluorobenzy)amino]-1-nitrobenzene gave 2-amino-4-[(4-fluorobenzyl)amino]-1-[(ethoxycarbonyl)amino]benzene [ethyl [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]carbamate] (II); II dihydrochloride was obtained in 73% yield.

L5 ANSWER 51 OF 59 USPATFULL on STN

ACCESSION NUMBER:	2003:81828 USPATFULL
TITLE:	Modifications of 2-amino-4-(4-fluorobenzylamino)-1-ethoxycarbonylaminobenzene, and processes for their preparation
INVENTOR(S):	Meisel, Peter, Dresden, GERMANY, FEDERAL REPUBLIC OF Landgraf, Karl-Friedrich, Dresden, GERMANY, FEDERAL REPUBLIC OF Schafer, Jurgen, Radebeul, GERMANY, FEDERAL REPUBLIC OF Thiel, Wilfried, Langebuuch, GERMANY, FEDERAL REPUBLIC OF Rischer, Matthias, Maintal, GERMANY, FEDERAL REPUBLIC OF Olbrich, Alfred, Halle/Westf., GERMANY, FEDERAL REPUBLIC OF Kutscher, Bernhard, Maintal, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S):	Asta Medica Aktiengesellschaft, Dresden, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6538151	B1	20030325
APPLICATION INFO.:	US 1998-181671		19981029 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-4926, filed on 9 Jan 1998, now patented, Pat. No. US 5914425		

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1997-19701694	19970120

DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Davis, Brian
LEGAL REPRESENTATIVE:	Venable, Hobbs, Ann S.
NUMBER OF CLAIMS:	4
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT:	259

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel modifications of the compound 2-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene of the ##STR1##

processes for their preparation and their use in pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 52 OF 59 USPATFULL on STN
ACCESSION NUMBER: 2002:323226 USPATFULL
TITLE: Methods for treating hyperactive gastric motility
INVENTOR(S): Argentieri, Thomas M., Yardley, PA, UNITED STATES
PATENT ASSIGNEE(S): Wyeth, Madison, NJ (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002183395	A1	20021205
APPLICATION INFO.:	US 2002-114148	A1	20020402 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-281471P	20010404 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: George M. Tarnowski, 5 Giralda Farms, Madison, NJ, 07940
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 719
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods and pharmaceutical compositions for treating, inhibiting or preventing hyperactive gastric motility in a mammal utilizing agonists of KCNQ potassium channels, including KCNQ2, KCNQ3, KCNQ4 and KCNQ5 potassium channels, alone or in combination. The hyperactive gastric motility may be associated with maladies including, colitis, irritable bowel syndrome and Crohn's disease. Compounds useful in these methods include the 1,2,4-triamino-benzene derivatives described in U.S. Pat. No. 5,384,330 (Dieter et al.) and the substituted 3-phenyl oxindole compounds described in U.S. Pat. No. 5,565,483 (Hewawasam et al.). Among the preferred compounds of this invention is N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also referred to as retigabine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 53 OF 59 USPATFULL on STN
ACCESSION NUMBER: 2002:283127 USPATFULL
TITLE: Modulatory binding site in potassium channels for screening and finding new active ingredients
INVENTOR(S): Rundfeldt, Chris, Coswig, GERMANY, FEDERAL REPUBLIC OF
Netzer, Rainer, Hamburg, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Radebeul, GERMANY, FEDERAL REPUBLIC OF (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6472165	B1	20021029
APPLICATION INFO.:	US 1999-368314		19990803 (9)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Guzo, David
ASSISTANT EXAMINER: Leffers, Jr., Gerald G.
LEGAL REPRESENTATIVE: Fulbright & Jaworski L.L.P.
NUMBER OF CLAIMS: 11
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 0 Drawing Figure(s); 0 Drawing Page(s)

LINE COUNT: 611
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A selective modulatory retigabine binding potassium channel receptor site containing subunits KCNQ2 and KCNQ3, and a method for directly selectively modulating that receptor site by administering retigabine to a cell preparation of the potassium channel.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 54 OF 59 USPATFULL on STN
ACCESSION NUMBER: 2002:206680 USPATFULL
TITLE: Methods of treating anxiety disorders
INVENTOR(S): Bowlby, Mark R., Richboro, PA, UNITED STATES
Rosenzweig-Lipson, Sharon J., East Brunswick, NJ, UNITED STATES
PATENT ASSIGNEE(S): American Home Products Corporation, Madison, NJ (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002111379	A1	20020815	
	US 6589986	B2	20030708	
APPLICATION INFO.:	US 2001-22579	A1	20011217	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-256834P	20001220 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WYETH, FIVE GIRALDA FARMS, MADISON, NJ, 07940
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 336
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods for treating, preventing or inhibiting anxiety, anxiety-related conditions and phobias in a mammal using compounds of the formula: ##STR1##

wherein: R.sub.1 is H, alkyl, alkanoyl or the radical Ar; R.sub.2 is H or alkyl; R.sub.3 is alkoxy, NH.sub.2, alkylamino, dialkylamino, amino substituted by the radical Ar, alkyl, alkenyl, alkynyl, or the radicals Ar or ArO--; R.sub.4 is H, alkyl or the radical Ar; R.sub.5 is H or alkyl or the radical Ar; or a pharmaceutically acceptable salt or ester form thereof; Ar is an optionally substituted phenyl radical; and n is 0 or 1, or a pharmaceutically acceptable salt or ester form thereof, with the methods particularly including the use of N-[2-amino-4-(4-fluorobenzylamino)-phenyl]carbamic acid ethyl ester, also known as retigabine.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 55 OF 59 USPATFULL on STN
ACCESSION NUMBER: 2002:26885 USPATFULL
TITLE: Pharmaceutical formulations and method for making
INVENTOR(S): Hoffmann, Torsten, Radebeul, GERMANY, FEDERAL REPUBLIC OF
Pieroth, Michael, Weinbohla, GERMANY, FEDERAL REPUBLIC OF
Zessin, Gerhard, Halle/Saale, GERMANY, FEDERAL REPUBLIC OF
Landgraf, Karl-Friedrich, Dresden, GERMANY, FEDERAL REPUBLIC OF

	NUMBER	KIND	DATE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002015730	A1	20020207
APPLICATION INFO.:	US 2001-793936	A1	20010227 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-187962P	20000309 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Gabriel P. Katona L.L.P., 14th Floor, 708 Third Avenue, New York, NY, 10017
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Page(s)
LINE COUNT: 995
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to an oral pharmaceutical formulation with variably adjustable release rate, which comprises one or more active ingredients, and one or more sucrose ester of a fatty acid as the sole release-controlling agent for said active ingredient wherein when the dosage form is a granule or a pellet, the formulation is made by melting the oral formulation, and granulating or pelletizing the melt.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 56 OF 59 USPATFULL on STN
ACCESSION NUMBER: 1999:69814 USPATFULL
TITLE: Modifications of 2-amino-4-(4-5fluorobenzylamino)-1-ethoxycarbonylaminobenzene, and processes for their preparation
INVENTOR(S): Meisel, Peter, Dresden, Germany, Federal Republic of
Landgraf, Karl-Friedrich, Dresden, Germany, Federal Republic of
Schafer, Jurgen, Radebeul, Germany, Federal Republic of
Thiel, Wilfried, Langebuuch, Germany, Federal Republic of
Rischer, Matthias, Maintal, Germany, Federal Republic of
Olbrich, Alfred, Halle/Westf., Germany, Federal Republic of
Kutscher, Bernhard, Maintal, Germany, Federal Republic of
PATENT ASSIGNEE(S): ASTA Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5914425		19990622
APPLICATION INFO.:	US 1998-4926		19980109 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1997-19701694	19970120

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Burn, Brian M.
ASSISTANT EXAMINER: Davis, Brian J.
LEGAL REPRESENTATIVE: Pillsbury Madison & Sutro LLP
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 5 Drawing Page(s)
LINE COUNT: 295
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to novel modifications of the compound

2-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene of the formula I ##STR1## processes for their preparation and their use in pharmaceutical compositions.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 57 OF 59 USPATFULL on STN

ACCESSION NUMBER:	1998:159983 USPATFULL
TITLE:	Use of 2-4-amino-4-(4-fluorobenzylamino) (-1-ethoxy-carbonylaminobenzene for the prophylaxis and treatment of the neurodegenerative disorders
INVENTOR(S):	Rostock, Angelika, Dresden, Germany, Federal Republic of Rundfeldt, Chris, Coswig, Germany, Federal Republic of Tober, Christine, Weinbohla, Germany, Federal Republic of Bartsch, Reni, Dresden, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5852053		19981222	
APPLICATION INFO.:	US 1996-736166		19961028	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1995-19539861	19951026

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Jordan, Kimberly
LEGAL REPRESENTATIVE:	Cushman Darby&Cushman IP Group of Pillsbury Madison & Sutro LLP
NUMBER OF CLAIMS:	14
EXEMPLARY CLAIM:	1
LINE COUNT:	260

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of the compound I ##STR1## or its pharmaceutically utilizable salts for the propylaxis and treatment of the squelae of chronic reduced cerebral blood supply, in particular of stroke, and for the treatment of nuerodegenerative disorders is claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 58 OF 59 USPATFULL on STN

ACCESSION NUMBER:	1998:157390 USPATFULL
TITLE:	Use of 4-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene for the prophylaxis and treatment of reduced cerebral blood supply
INVENTOR(S):	Rostock, Angelika, Dresden, Germany, Federal Republic of Rundfeldt, Chris, Coswig, Germany, Federal Republic of Tober, Christine, Weinbohla, Germany, Federal Republic of Bartsch, Reni, Dresden, Germany, Federal Republic of
PATENT ASSIGNEE(S):	Asta Medica Aktiengesellschaft, Dresden, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5849789		19981215	
APPLICATION INFO.:	US 1997-937420		19970925	(8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1996-736166, filed on 28 Oct 1996			

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1995-19539861	19951026

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Jordan, Kimberly
LEGAL REPRESENTATIVE: Cushman Darby&Cushman IP Group of Pillsbury Madison & Sutro LLP
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 252
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The use of the compound I ##STR1## or its pharmaceutically utilizable salts for the propylaxis and treatment of the sequel of chronic reduced cerebral blood supply, in particular of stroke, and for the treatment of neurodegenerative disorders is claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 59 OF 59 USPATFULL on STN
ACCESSION NUMBER: 95:7895 USPATFULL
TITLE: Pharmaceutically active 1,2,4-triamino-benzene derivatives, processes for their preparation and pharmaceutical compositions containing them
INVENTOR(S): Dieter, Hans-Reinhold, Darmstadt, Germany, Federal Republic of
Engel, Jurgen, Alzenau, Germany, Federal Republic of
Kutscher, Bernhard, Maintal, Germany, Federal Republic of
Polymeropoulos, Emanuel, Frankfurt, Germany, Federal Republic of
Szelenyi, Stefan, Schwaig, Germany, Federal Republic of
Nickel, Bernd, Muhltal, Germany, Federal Republic of
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5384330		19950124	
APPLICATION INFO.:	US 1993-2458		19930108	(8)

	NUMBER	DATE
PRIORITY INFORMATION:	DE 1992-4200259	19920108

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Dees, Jose G.
ASSISTANT EXAMINER: Barts, Samuel
LEGAL REPRESENTATIVE: Cushman, Darby & Cushman
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 700
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmacologically active 1,2,4-triaminobenzene derivatives of the General Formula I: ##STR1## where the symbols R1' R2' R3' R4' R5' Ar and Alk have the following meanings:

where the symbols R.sub.1, R.sub.2, R.sub.3, R.sub.4, R.sub.5, Ar and Alk have the following meanings:

R.sub.1 : hydrogen, C.sub.1 -C.sub.6 -alkyl, C.sub.2 -C.sub.6 -alkanoyl or the radical Ar;

R.sub.2 : hydrogen or C.sub.1 -C.sub.6 -alkyl;

R.sub.3 : C.sub.1 -C.sub.6 -alkoxy, NH.sub.2, C.sub.1 -C.sub.6 -alkylamino, C.sub.1 -C.sub.6 -dialkylamino, amino substituted by the radical Ar, C.sub.1 -C.sub.6 -alkyl, C.sub.2 -C.sub.6 -alkenyl, C.sub.2 -C.sub.6 -alkynyl, the radical Ar or the radical ArO--;

R.sub.4 : hydrogen, C.sub.1 -C.sub.6 -alkyl or the radical Ar;

R.sub.5 : hydrogen or C.sub.1 -C.sub.6 -alkyl or the radical Ar;

Alk: a straight or branched alkylene group containing 1-9 carbon atoms, which can also be substituted by the radical Ar.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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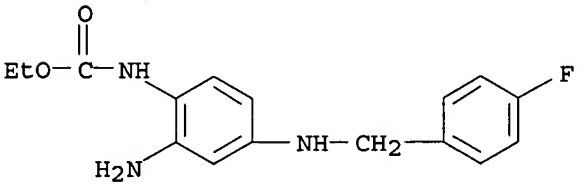
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 150812-12-7 REGISTRY
CN Carbamic acid, [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN D 23129
CN Ethyl [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]carbamate
CN **Retigabine**
FS 3D CONCORD
MF C16 H18 F N3 O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMLIST, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE, PHAR, PROMT, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

49 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
51 REFERENCES IN FILE CAPLUS (1907 TO DATE)